KU’s Frontiers CTSA and Developing Informatics Capabilities

Russ Waitman, PhD
Associate Professor, Director Medical Informatics
Department of Biostatistics
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“It is the responsibility of those of us involved in today’s biomedical research enterprise to translate the remarkable scientific innovations we are witnessing into health gains for the nation.”
Background:
NIH Goal to Reduce Barriers to Research

- Administrative bottlenecks
- Poor integration of translational resources
- Delay in the completion of clinical studies
- Difficulties in human subject recruitment
- Little investment in methodologic research
- Insufficient bi-directional information flow
- Increasingly complex resources needed
- Inadequate models of human disease
- Reduced financial margins
- Difficulty recruiting, training, mentoring scientists
CTSA Objectives:

The purpose of this initiative is to assist institutions to forge a uniquely transformative, novel, and integrative academic home for Clinical and Translational Science that has the consolidated resources to:

1) captivate, advance, and nurture a cadre of well-trained multi- and inter-disciplinary investigators and research teams;

2) create an incubator for innovative research tools and information technologies; and

3) synergize multi-disciplinary and inter-disciplinary clinical and translational research and researchers to catalyze the application of new knowledge and techniques to clinical practice at the front lines of patient care.
Current Funded CTSA Programs

Currently, 46 institutions are part of the consortium, spanning 28 states and a broad range of scientific expertise. Consortium members represent each geographic region of the country. When fully implemented, 60 institutions will be linked together to energize the discipline of clinical and translational science.
Frontiers Principal Investigators

Richard J. Barohn, MD
Program Director, GCRC
Chairman, Department of Neurology
Gertrude and Dewey Ziegler Professor of Neurology
Director, Frontiers

Lauren S. Aaronson, PhD, RN, FAAN
Professor, School of Nursing
Professor, Department of Health Policy and Management, School of Medicine
Deputy Director, Frontiers
Frontiers Organizational Structure

Chancellor, KU
B. Gray-Little

Executive Vice Chancellor, KUMC
B. Atkinson

Heartland Institute for Clinical &
Translational Research (HICTR)
Clinical Research Development Office
(CReDO)

HICTR Director/Co-PI, R. Barohn

HICTR Deputy Director/Co-PI,
and CReDO Director
L. Aaronson

Administrative Director
for Operations & Finances
J. Otey

Clinical & Translational Research
Education Center
Director: Ellerbeck

Biomedical Informatics
Director: Waitman

Biostatistics
Director: Mayo

Participant & Clinical Interactions
Resources Program
Director: Burns

Novel Methods 1: Institute
for Advancing Medical
Innovations
Director: Weir

Translational Technologies
Resource Center
Director: Brooks

Novel Methods 2: Personalized Medicine/
Outcomes Center
Director: Spertus

Pilot and Collaborative Studies
Funding Program
Director: Kopf

Community Partnership for Health
Program (Community Engagement)
Director: Kopf

Regulatory Knowledge & Support
Director: Kopf

Ethics Program
Director: Lantos

Evaluation: RDI, W. Boulden
Current Strengths at KU

- Rich history of reaching frontiers of Kansas with educational, research, and health care programs
- Wealth of networks available
- Exceptional School of Pharmacy and new IAMI
- Successful multi-disciplinary community-based research programs on which to build
- Existing support programs of RI, Office of Grants & Research for SON and SAH, Compliance program
- Community support (philanthropic and JCERT)
- Recent investments in clinical research (e.g., GCRC, informatics)
Overall Frontiers Specific Aims

1. Create a new academic home with innovative education and training programs for clinical and translational investigators that will transform the type, and increase the number, of faculty and investigators needed to bring discoveries and research findings more rapidly to the point of care;

2. Provide an enhanced coordinated translational research infrastructure that will speed the process from discovery to community research in Kansas and the Kansas City region; and

3. Actively engage the community in developing, testing, and disseminating translational research through existing and new networks in Kansas and the Kansas City region.
The CTSA Grant Will Allow Us To:

- Change the culture to support more investigators to do clinical and translational research
- Become part of the national CTSA consortium
  - Allow us to apply for future NIH grants that are restricted to CTSA sites.
  - Provide increased opportunities for cross institutional collaborations within CTSA consortium.
- Maintain current programs
  - Former GCRC
  - Former K30
  - Continue Biostatistics support for initial consultation
- Expand current programs
  - Additional funds for clinical pilots grants
  - Former K30 plus new training programs (KL2 and T32)
- Develop and expand comprehensive Informatics program
Frontiers Developments to Date

- Initiated discussions with Kauffman Foundation that led to IAM1 funding program
- Formalized collaborative relations with regional schools and health systems
- Launched Medical Informatics Program
  - Velos
  - Participant Registry Program
  - Recruited Russ Waitman
  - HERON and RAVEN
- Expanded GCRC to Support Pharma Trials in CTU
- Developed Research Coordinator Pool
- Integrating GCRC and CTU into the CTSA
## 2011 CTSA Budget

<table>
<thead>
<tr>
<th>Program</th>
<th>Amount</th>
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<tbody>
<tr>
<td>HICTR Administration</td>
<td>$409,904</td>
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<tr>
<td>Clinical &amp; Translational Education Center (CTREC)</td>
<td>$1,052,600</td>
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<tr>
<td>Biomedical Informatics</td>
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<td>Biostatistics</td>
<td>$173,526</td>
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<td>Community Partnership for Health (CPH)</td>
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<td>NM1: Institute for Advancing Medical Innovations (NM1: IAMI)</td>
<td>$0</td>
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<td>NM2: Personalized Medicine &amp; Outcomes Center (NM2: PMOC)</td>
<td>$96,416</td>
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<td>Translational Technologies Resource Center</td>
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<td>Pharmocokinetics/Pharmacodynamics Program</td>
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<td>Pilot and Collaborative Funding Studies Program</td>
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<td>Participant &amp; Clinical Interaction Resources Program (PCIRP)</td>
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<td>Regulatory Knowledge and Support Program</td>
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<td>Ethics Program</td>
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<td>Implementation and Evaluation</td>
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<td>Total</td>
<td>$4,000,000</td>
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</table>
Developing CTSA Informatics Capabilities: Existing Teams

- Clinical Research & Medical Informatics
  - CRIS: Comprehensive Research Information System Team
  - New Medical Informatics plus KUMC Information Resources critical contributors for infrastructure
- Bioinformatics
  - K-INBRE Bioinformatics Core
  - Center for Bioinformatics and Engineering School
  - Dr. Gerry Lushington
- Center for Health Informatics
  - World Class Telemedicine
  - Leading Health Information Exchange for the State
  - Terminology, Training, Simulation Expertise
  - Dr. Judith Warren
Frontiers Informatics Aims

1. Provide a HICTR portal for investigators to access clinical and translational research resources, track usage and outcomes, and provide informatics consultative services.

2. Create a platform, HERON (Healthcare Enterprise Repository for Ontological Narration), to integrate clinical and biomedical data for translational research.

3. Advance medical innovation by linking biological tissues to clinical phenotype and the pharmacokinetic and pharmacodynamic data generated by research cores in phase I and II clinical trials (addressing T1 translational research).

4. Leverage an active, engaged statewide telemedicine and Health Information Exchange (HIE) effort to enable community based translational research (addressing T2 translational research).
Aim #1: Create a Portal and Consult

- Bring together existing resources
  - Translational Technologies Resource Center
- Link to national resources
  - [www.vivo.org](http://www.vivo.org) – Facebook for researchers
  - [www.eagle-i.org](http://www.eagle-i.org) – National resources (rodents, RNAi, to patient registries)
- Develop tools to measure and track our investment
  - Pilot funding requests, electronic Institutional Review Board process
- Provide a hands on informatics consult service
  - Also organize existing resources
VICTR Funding Requests

All VICTR funding requests are managed through StarBRITE. Research teams may petition for any amount of funding through our “Pick List” application.

Scientific justification and review level is triggered by the amount of funding requested through the “Pick List”
Aim #2: Create a data “fishing” platform

- Develop business agreements, policies, data use agreements and oversight.

- Implement open source NIH funded (i.e. i2b2) initiatives for accessing data.

- Transform data into information using the NLM UMLS Metathesaurus as our vocabulary source.

- Link clinical data sources to enhance their research utility.
A. Develop business agreements, policies, data use agreements and oversight.

- September 2010 the hospital, clinics and university signed a master data sharing agreement to create the repository.
  - Executive Committee – decides organization/systems expansion
  - Data Request Oversight Committee – guides implementation and approves/monitors use.

- Use Cases:
  - After signing a system access agreement, cohort identification queries and view-only access is allowed but logged and audited
  - Requests for de-identified patient data, while not deemed human subjects research, are reviewed.
  - Identified data requests require approval by the Institutional Review Board prior to data request review.
  - Contact information from the Frontiers Participant Registry have their study request and contact letters reviewed by the Participant and Clinical Interactions Resources Program
HERON: Repository Architecture

Participants
Clinical Systems
(EPIC, IDX, VELOS)

Information in files from Source Systems
(Ex: archived database extracts or HL7 messages)

Extract, Transform & Load Processes or HL7 Listeners

Identified staging database (Night HERON)

De-identification & Transform Processes

De-identified staging database (Blue HERON)

Identified data server

De-identified data server

I2b2 clinical business intelligence application
(JBoss, VMWare virtualized host managed by KUMC Information Resources)

Clinical/Translational Researcher
HERON De-identification Decisions

- HIPAA Safe Harbor De-identification
  - Remove 18 identifiers and date shifting by 365 days back
  - Resulting in non-human subjects research data but treated as a limited data set from a system access perspective. System users and data recipients agree to treat as a limited data set (acknowledging re-identification risk)

- To be addressed:
  - For now, we won’t add free text such as progress notes with text scrubbers (DeID, MITRE Identification Scrubber toolkit)
  - Currently have “obfuscation” turned on.
    - No sets < 10 and sets randomly perturbed ± 3 patients
  - While de-identified, access to timeline functionality provides individualized patient “signatures”
C. Transform data into information using standard vocabularies and ontologies

- NIH Goal: break down silos and “administrative bottlenecks”
  - foreshadowed meaningful use?
- Vocabulary dialects
  - Local: Serum Potassium is ComponentID 2002 at KUH
  - Vendor: Lorazepam 0.5MG tab is First DataBank gcn seqno 3757
  - Standard: Lorazepam 0.5MG tab is RxNorm CUI 197900, UMLS CUI C0689398
- What’s an ontology?
- "formal, explicit specification of a shared conceptualization"
Other Key HERON decision

- “Lazy” Load supports alternative views of reality
  - Load with the local terminology first. Map concepts to standards secondarily in the concept space.
  - Allows multiple ontologies for observations and works around mapping challenges with contributing organizations

Further technical details described at: http://informatics.kumc.edu/work/wiki/HERON
### D. Link clinical data sources to enhance their research utility.

<table>
<thead>
<tr>
<th>Data source</th>
<th>System “Go-Live” Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient/Emergency demographics, “ADT” locations &amp; services</td>
<td>2006</td>
</tr>
<tr>
<td>Inpatient diagnoses (DRG, ICD9)</td>
<td>1990</td>
</tr>
<tr>
<td>Outpatient visits services, diagnoses, procedures (ICD, CPT)</td>
<td>2002</td>
</tr>
<tr>
<td>Laboratory Results (inpatient/outpatient)</td>
<td>2007</td>
</tr>
<tr>
<td>Electronic Medication Administration Record (eMAR)</td>
<td>2007</td>
</tr>
<tr>
<td>Inpatient vitals, inputs, outputs and discrete observations</td>
<td>2007</td>
</tr>
<tr>
<td>Clinical Research Information System – clinical trials</td>
<td>2007</td>
</tr>
<tr>
<td>Provider Order Entry</td>
<td>2010</td>
</tr>
<tr>
<td>Problem List and Provider Notes</td>
<td>2009</td>
</tr>
<tr>
<td>Surgical Pathology</td>
<td>2002</td>
</tr>
<tr>
<td>Microbiology, Cardiology, Radiology</td>
<td>2006</td>
</tr>
<tr>
<td>Medication reconciliation</td>
<td>2007</td>
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<tr>
<td>Tumor Registry, BSR</td>
<td>1994</td>
</tr>
<tr>
<td>REDCap investigator initiated patient registries</td>
<td>2011</td>
</tr>
<tr>
<td>Perioperative schedule and indicators</td>
<td>2005</td>
</tr>
<tr>
<td>Social Security Death Indicator</td>
<td>1930s?</td>
</tr>
<tr>
<td>Medicaid databases</td>
<td>2005</td>
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</table>
Developing a Rich Description of our Population: Existing and Planned Data Sources for HERON. Existing sources shown in **bold underlined text** and planned in plain text.
An i2b2 query against HERON for currently supported cancer centric data sources

Any neoplasm ICD9 diagnosis (106,000 patients) and a WBC count (121,000) -> 44,000 distinct patients,
*require height (123,000) and weight (154,000) -> 35,000 patients,
•require Wong-Baker pain scale (84,000) -> 14468 patients,
•Body Temperature (158,000) -> 14463 patients,
•Surgical Pathology Procedures CPT (85,000) -> 12446 patients,

Finally selective serotonin 5-HT3 antagonist antiemetics -> 8517 patients
With our improved hardware (Fusionio memory cards), the cohort size is returned in 15 seconds for this 8 group query.
Aim #3: Link biological tissues to clinical phenotype and our research cores’ results

- Support Cancer Center, IAMI, and bridge to Lawrence Research
- **First focus**: Incorporate clinical pathology and biological tissue repositories with HERON and CRIS to improve cohort identification, clinical trial accrual, and improved clinical trial characterization
  - Aligned with existing enterprise objectives to improve biological tissue repository information systems
  - Clinical trial accrual identified by many as a weak point institutionally
  - Target both biological research specimens and routine clinical pathology
Aim #3: Link biological tissues to clinical phenotype and our research cores’ results

- **Second focus:** Support IAMI clinical trials by integrating and standardizing information between bioinformatics and pharmacokinetic/pharmacodynamic (PK/PD) program and the Comprehensive Research Information System (CRIS)
  - Clinical research findings, clinical records, and research laboratory results are not integrated.
  - PK/PD should be the most common research analysis for phase 1 trials.

- **Third focus:** Apply molecular bioinformatics methods to enhance T1 translational research in areas such as molecular biomarker discovery efforts and pharmaceutical lead optimization
  - Also promote clinical domains for Lawrence researchers
Aim #4: Leverage telemedicine and Health Information Exchange (HIE) for community based translational research

- The HITECH Act and “meaningful use” are a landmark event for Biomedical Informatics and Health Information Technology
  - State Health Information Exchanges
  - Regional Extension Centers
  - Incentives (then penalties) for Providers
- Provide health informatics leadership to ensure state and regional healthcare information exchange (HIE) and health information technology initiatives foster translational research
  - Dr. Connors chaired the formation Kansas Health Information Exchange
  - Drs. Greiner and Waitman also participated in KHPA and Regional Extension Center Activities
- Engage so research has a place at the table
Unique Combination of Telemedicine for Community Research and CRIS

<table>
<thead>
<tr>
<th>Title</th>
<th>PI</th>
<th>Grant/Agency</th>
<th>CRIS used?</th>
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<tbody>
<tr>
<td>Describing and Measuring Tobacco Treatment in Drug Treatment</td>
<td>K. Richter</td>
<td>R21DA020489, National Institute on Drug Abuse</td>
<td>Yes</td>
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<td>Telemedicine for Smoking Cessation in Rural Primary Care</td>
<td>K. Richter</td>
<td>R01HL087643, NIH National Heart, Lung and Blood Institute</td>
<td>No</td>
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<td>Using CBPR to Implement Smoking Cessation in an Urban American Indian Indian Community</td>
<td>C. Daley</td>
<td>R24MD002773, National Center on Minority Health and Health Disparities</td>
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<td>Centralized Disease Management for Rural Hospitalized Smokers</td>
<td>E. Ellerbeck</td>
<td>R01CA101963, National Cancer Institute</td>
<td>Yes</td>
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<tr>
<td>Pediatric epilepsy prevalence study</td>
<td>D. Lindeman</td>
<td>RTOI # 2008-01-01 AUCD, National Center for Birth Defects and Developmental Disabilities, CDC</td>
<td>No</td>
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<tr>
<td>Kansas Comprehensive Telehealth Services for Older Adults</td>
<td>E-L Nelsen, L. Redford</td>
<td>Health Resources and Services Administration Office for the Advancement of Telehealth</td>
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</tr>
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</table>

Promote capability for subject engagement and facilitate collaboration via tele-research meetings
“Wire” clinical information systems to provide a laboratory for translational informatics research

**KUH/UKP EMR Rollout**

- Disseminate translational research findings and evidence in the clinical workflow
- **The “last” mile**: measure the translation’s adoption
Engage with community providers adopting EHRs as a platform for translational research.

- Alignment with State Medicaid Goals
  - KHPA primary goal for the State Medicaid HIT Plan (SMHP): implementing a medical home for all Medicaid recipients
  - Unique compared with other states: current incentives in HITECH may promote information disparities
- Partner with Regional Extension Center
  - Their mission is to be the consultants on the ground helping providers adopt and use systems
- The Kansas Physicians Engaged in Practice Research (KPEPR) Network
  - pilot connections between rural clinical systems and HERON to evaluate clinical research in rural settings
Collaborate with the Personalized Medicine and Outcomes Center (PMOC)

- Enhance data maintained by the state, national registries, and regional collaborators
  - State Medicaid, State Employees, Social Security Death Indexes, Educational databases, Nursing Quality Indicators
  - Will likely involved distributed methods of data integration as opposed to explicit management of all datasets.
- Collaborate with the PMOC to provide complex risk models for decision support to other clinical specialties and settings
  - Current focus is customized informed consent forms for cardiology procedures (bare metal versus drug eluting stent)
  - Target integration with EPIC in latter years of CTSA grant.
Questions?